

### REMARKS

Reconsideration and allowance are respectfully requested.

Claims 1-14 are pending. Non-elected claims 11-14 were withdrawn from consideration by the Examiner. New claims 15-20 are added.

The amendments to claims 1-2 are supported, inter alia, by Examples 1-2. Thus, no new matter has been added by the claim amendments. The original subject matter of claims 3 and 6 is canceled without prejudice or disclaimer because the limitation are redundant in view of the amendment of the independent claims. Those claims are amended to duplicate the limitations of claims 4-5 but with different claim dependency. Claims 7-10 are amended to conform to U.S. practice. New claims 15-18 duplicate the limitations of claims 7-10 but dependent from independent claim 2. New claims 19-20 are directed to detection of one or more mutations in the *POLG* gene with a diagnostic/genetic technique involving amplification.

The title has been amended to be descriptive of the claimed invention.

#### *35 U.S.C. 112 – Enablement*

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 1-10 were rejected under Section 112, first paragraph, because it was alleged that "[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with [the] claims." Applicants traverse.

The Examiner stated on page 4 of the Action that the specification is enabling for methods for the diagnosis of male infertility and the screening for genetic predisposition to male infertility characterized by detecting homozygosity for the loss of *POLG* gene

function or the heterozygote which involve at least one mutation in the trinucleotide (CAG) microsatellite repeat through a genetic technique such as PCR. Applicants submit that claims 7-8, 15-16 and 19-20 are consistent with this finding of enablement.

It was further alleged on page 7 of the Action, "With respect to claims 9 and 10, it should be noted that the specification enables only nucleotide-based detection techniques for the diagnosis of male infertility." Applicants disagree because the specification on page 9 teaches detection techniques based on gene products (e.g., protein) as well as nucleic acids like DNA and RNA. Both are molecular techniques which have been subdivided in the past into genetic and biochemical methodologies. Here, Applicants have made an invention based on detection of mutation(s) in the trinucleotide (CAG) microsatellite repeat which necessarily involves a coding region of the *POLG* gene and results in detectable differences in mutant proteins encoded by their respective mutated *POLG* genes. Protein-based detection techniques can determine the presence or absence of wild-type protein and the altered size of mutant protein (e.g., molecular weight, mobility in chromatographic and spectroscopic separation, etc.). Therefore, Applicants submit that persons skilled in the art would be able to detect mutations at either the level of nucleic acid or protein. For example, genetic amplification techniques and protein-based biochemical techniques such as Western analysis and immunologic methods are art-recognized alternatives for determining the effect of a mutation on the *POLG* gene directly (genetic techniques) or the gene product encoded by the *POLG* gene (biochemical techniques) respectively.

Withdrawal of the enablement rejection made under Section 112, first paragraph, is requested because it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

### *35 U.S.C. 112 – Definiteness*

Claims 1-10 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse.

Claim 1-2 have been amended to recite steps in the method.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

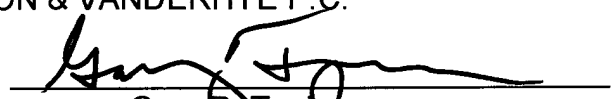
*Conclusion*

Having fully responded to all of the pending objections and rejections contained in the Office Action (Paper No. 62003), Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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